Multiscale Modeling of the Brain

New Approaches to Model Axonal Bundle Physics for Injury, Rehabilitation and Beyond

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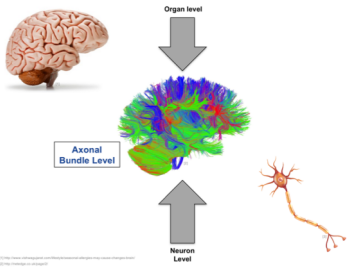
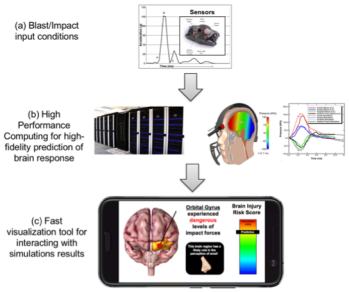
Introduction/Objectives

- Traumatic brain injury (TBI) is an widespread problem. In the United States, TBI affects both military and civilian populations.
- Studies have shown that 1.6 to 3.8 million individuals in the United States experience a sports-related concussion annually, with a growing number of these concussions experienced by youth-sports participants.
- Almost 2% of the United States' population is currently living with TBI-related disabilities.
- Medical imaging needs to be leveraged better to represent the mesoscopic level of brain.



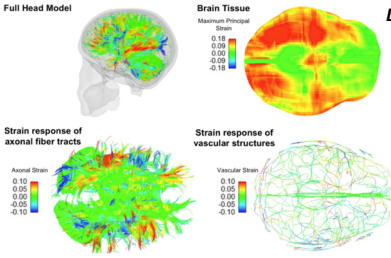


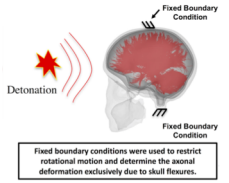
- We aim to leverage cloud resources to create personalized simulations that continuously monitors, analyzes and predicts the brain's response, referred to as the "*Digital Brain*".
- *Digital Brain* can be thought of as a digital copy of your brain that resides in the cloud which obtains data from wearable sensors, such as impact sensors or electroencephalogram (EEG), and uses physics-based methods to compute the brain's response.

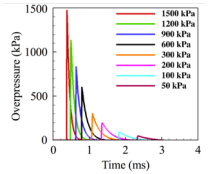
It is important to note that, currently, modeling is the only means to understand how external impact forces are translated into the brain – there is no other way to do this.

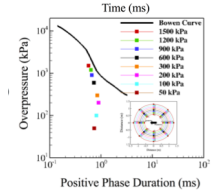
Results & Discussion

Do blast induced skull flexures result in axonal deformation?



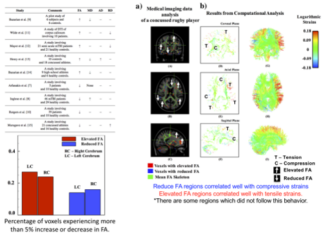




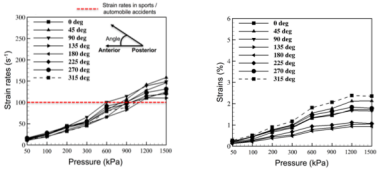


- The method was used to investigate the blast-induced skull flexure and its effect on axonal deformation.
- In addition, the directional effects of loading on the axonal response due to skull flexures were also investigated.
- Simulations suggest that skull flexures result in axonal deformation – causing low strain and potentially ***high strain rates***.

Tract Damage Validation

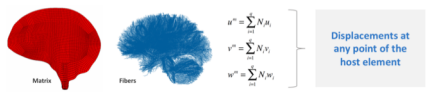


Preliminary observations show that elevated/reduced FA regions matched well with fibers experiencing tensile/compressive strains.



Methods

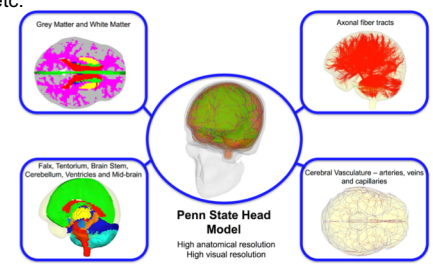
- The brain consists of a complex network of axonal fibers that can be observed through the use of magnetic resonance diffusion tensor imaging (MR-DTI).
- These fibers can be considered the mesoscopic level of the brain, smaller than the organ and larger than the individual cells.
- The **embedded element method**, a mesh superposition technique, is a method that allows for an explicit inclusion of the axonal fiber network into finite element models. This technique facilitates the inclusion of multiple fibers per finite element.
  - Explicit meshing enables us to track each individual axonal fiber tract.
  - Localized axonal deformations can be studied.
  - Fast method to include complex fiber networks
  - Offers no limitations when locations and orientations are arbitrary.
  - Multiple fibers can be included in a single "matrix" element.
  - Because axonal fibers are meshed, the method can handle multiple physics, e.g. electromagnetics, diffusional processes, etc.



Desirable when complex reinforcement details are present and large amount of reinforcements are present.

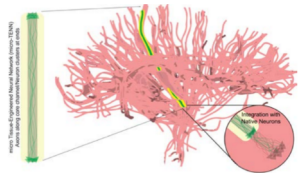
$$\mathbf{K}^e = \int_{host} \mathbf{B}^{eT}\mathbf{D}_c\mathbf{B}^e \cdot dV + \int_{embedded} \mathbf{B}^{eT}\mathbf{T}_e^T\mathbf{D}_c\mathbf{T}_e\mathbf{B}^e \cdot dV$$

K	B	D	$\mathbf{T}_e$
Stiffness matrix	Strain displacement matrix of the parent element	Elasticity matrix	Transformation matrix of strains from global to local

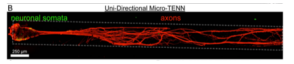


Bridging Scales

In collaboration with Kacy Cullen at UPenn, we are developing computational methods to optimize and design micro-tissue engineered neural networks (micro-TENNs)

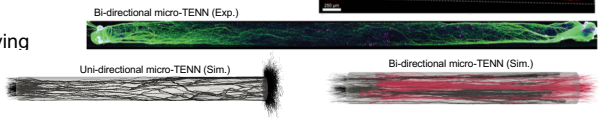


Micro-TENNs can be thought of as axonal tracts that may restore function



Objectives

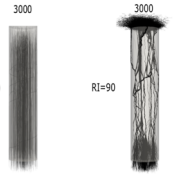
- Quantify the structural and electric properties of micro-TENNs
- Process the input and output of living electrodes precisely in real time



Approach

- **Computationally grow** the Micro TENNs to get the morphology and connectivity details
- **Simulation and analysis** of spiking neuron networks

Our computational growth model can capture similar features as real micro-TENNs



Acknowledgments & References

- *Funding:* Brain Initiative U01-NS094340 (Cullen & Kraft), W81XWH-14-C-0045, DOTC-17-01-INIT0086
- Center Brain image from https://www.yourgenome.org/stories

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